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The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SUSAN I. HERSHENSON

Appeal No. 1997-2133
Application 08/172,507

ON BRIEF

Before WILLIAM F. SMITH, LORIN and MILLS, Administrative Patent Judges,
MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final
rejection of claims 1-13, which are all of the claims pending in this application.

We reverse.

Claims 1-7 and 9 are illustrative of the claims on appeal and read as follow:

1. A lyophilized stem cell factor SCF formulation containing histidine.
2. A lyophilized SCF formulation containing glutamic acid.
3. A lyophilized SCF formulation of claim 1 or 2 wherein said formulation contains sucrose.
4. A lyophilized SCF formulation of claims 1 or 2 wherein said formulation contains mannitol.
5. A lyophilized SCF formulation containing histidine and glutamic acid.
6. A lyophilized SCF formulation of claim 5 further containing sucrose.
7. A lyophilized SCF formulation of claim 5 further containing mannitol.
9. A method for preparing lyophilized SCF formulation comprised of the steps of:
(a) mixing said SCF in a buffer containing an amino acid or amino acids selected from the group consisting of histidine and glutamic acid; and
(b) lyophilizing said SCF.

The prior art references of record relied upon by the examiner in rejecting the
appealed claims are:

Lee	0 314 095	Oct. 26, 1988
Zsebo et al. (Zsebo)	91/05795	Sep. 28, 1990
(European Patent Application)		
Audhya	90/12029	Apr. 9, 1990
Morimoto	2,014,009	Oct. 07, 1990

OPINION

In reaching our decision in this appeal, we have given careful consideration to the appellant's specification and claims, to the applied prior art references, and to the respective positions articulated by the appellant and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellant regarding the above-noted rejection, we make reference to the examiner's answer (Paper No. 20, mailed December 6, 1996) for the examiner's complete reasoning in support of the rejection, and to the appellant's brief (Paper No. 18, filed September 18, 1996) for the appellant's arguments thereagainst. As a consequence of our review, we make the determinations which follow.

DECISION ON APPEAL

35 U.S.C. 103

Claims 1-13 stand rejected under 35 U.S.C. 103 as obvious in view of Zsebo taken with Lee, Audhya and Morimoto.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532,

28 USPQ2d 1955, 1956 (Fed. Cir. 1993). Rejection of claimed subject matter as obvious under 35 U.S.C. § 103 in view of a combination of prior art references requires consideration of whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that such person would have reasonable expectation of success; both the suggestion and reasonable expectation of success must be founded in prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

Zsebo indicates that stem cell factor may be formulated in a composition which is lyophilized, and that ingredients in the composition such as lactose and mannitol may function as bulking agents or tonicity modifiers. The examiner acknowledges that Zsebo does not disclose the addition of histidine or glutamic acid as stabilizers for stem cell factor.

Lee is relied on for the disclosure that lyophilized plasma proteins, such as factor VIII, may be stabilized in a formulation which includes sodium chloride and calcium chloride and the amino acid histidine as buffering agent. Lee also discloses that sugars such as mannitol, sucrose and mannose can be added prior to lyophilization. Lee, page 3, lines 10-11. Audhya discloses the addition of amino acids such as arginine, lysine, aspartic acid and glutamic acid to stabilize lyophilized proteins, such as thymopentin, thymoralin, growth hormone, enkephalin and tumor necrosis factor. Audhya, page 7, lines 16-17 and page 9,

lines 15-19. Morimoto describes that the protein urokinase can be stabilized using polar amino acids such as glutamic acid and histidine. Morimoto, page 4, last paragraph.

The examiner surmises that it would have been obvious to one of ordinary skill in the art at the time of the present invention to use the stabilizing amino acids glutamic acid and histidine of Lee, Audhya and Morimoto either alone or in combination to stabilize Zsebo's stem cell factor preparation prior to lyophilization because these amino acids are commonly used for such purposes. Examiner's Answer, page 5. It is also argued that it would have been obvious to determine all operable and optimal parameters of the formulation suggested by Zsebo, Lee, Audhya and Morimoto, such as pH and the concentration of the additives, because it is desirable to have the product formed in such a fashion that it is non-toxic, safe and easy to handle and administer; optimal formulations have such desirable characteristics. Examiner's Answer, page 6.

Appellant argues that no prima facie case of obviousness is made because no motivation to combine the teachings of the references is present, and there is no reasonable expectation of success. However, the test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art. See In re Young, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991) and In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). In evaluating such references it is proper to take into account not only the specific teachings of the references

but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. In re Preda, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The cited references all generally deal with the stabilization of lyophilized proteins.

We assume, arguendo, that a prima facie case of obviousness has been presented by the examiner, and thus the burden shifts to appellant to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991). Accordingly, we carefully evaluate the objective evidence of nonobviousness presented by the appellant.

Objective evidence of non-obvious presented by appellant includes teachings away in the prior art references from the claimed invention. These teachings away are urged to rebut any prima facie case of obviousness presented by the examiner.

Appellant's point is well taken that a prior art reference must be considered in its entirety, i.e. as a whole including portions which would lead away from the claimed invention. W.L. Gore & Associates, Inc., v. Garlock, Inc., 721 F.2d 1540, 1550, 220 USPQ 303 (Fed. Cir. 1983). Appellant submits, for example, that taking a careful look at Lee indicates that formulations containing histidine showed no biological activity and thus teach away from the claimed invention. Lee, Table IV, page 5. Brief, pages 16-17. It is also presented that Audhya teaches away from the use of sugars such as sucrose and mannitol,

and amino acids, such as asparagine, glucine and lysine for protein stabilization, since these were taught to be ineffective in stabilizing thymopentin protein. Audhya, page 7, lines 3-10.

Our reviewing court in In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994) stated:

[a] reference may be said to teach away when a person of ordinary skill, upon [examining] the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.

It would appear that persons of skill in the art may have been equally encouraged and discouraged from following the paths of the cited references. In this respect it would appear that there is some level of unpredictability in the relevant art.

Thus, appellant takes issue with the argument of the examiner that the addition of amino acids, alone or together for stabilization purposes would have been recognized as broadly applicable to any protein. Appellant argues that the peptides of Morimoto (urokinase), Lee (factor VIII) and Audhya (thymopentin) are fundamentally different than the claimed stem cell factor protein. It would appear on second review, that the cited references give no indication of which parameters are critical and no direction as to which of many possible

choices is likely to be successful in achieving a stabilized stem cell factor protein. The fact that the claimed combination falls within the scope of possible combinations taught therein does not render it unpatentably obvious. See In re O'Farrell, 853 F.2d 894, 903, 7 USPQ 2d 1673, 1681 (Fed. Cir. 1988).

Moreover, Appellant's arguments directed to the unexpected results obtained from the present invention are relevant. As stated in In re O'Farrell, 853 F.2d at 903, 7 USPQ2d at 1681:

There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious.

Appellant argues that the claimed invention provides an unexpected improvement in the level of stability of lyophilized stem cell factor, especially in view of the teachings away from the claimed invention found in the cited references. To support this position appellant relies on evidence presented in the specification, Example 1 and Figure 1. This evidence appears to show that stem cell factor samples buffered with glutamic acid, histidine and sucrose in varying combinations, are more stable and contain less cross-linked dimer degradation product than formulations of the same pH buffered with a single amino acid or non-amino acid (succinate). Brief, page 15.

After evidence or argument is submitted by the appellant in response to rejection based on obviousness, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of the argument. We have carefully studied the arguments and evidence of record. We agree with appellant that the cited references also include objective evidence of non-obvious, a teaching away from the claimed invention, which is sufficient to rebut the examiner's prima facie case of obviousness. On balance, we believe that the totality of the evidence presented by the examiner and appellant weighs in favor of non-obviousness of the claimed invention. The rejection of the claims for obviousness of the claimed invention is reversed.

CONCLUSION

The rejection of the claims under 35 U.S.C. § 103 for obviousness is reversed.

REVERSED

WILLIAM F. SMITH)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
HUBERT C. LORIN)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
Demetra J. Mills)	

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